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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
EXCHANGE PLACE
BOSTON, MA 02109-2881

EXAMINER	
KOSAR, ANDREW D.	
ART UNIT	**PAPER NUMBER**
1654	

MAIL DATE	DELIVERY MODE
10/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/706,100	FEIN, SEYMOUR H.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,7,9,27 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,7,9,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 November 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20071009*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Previous Office Action Withdrawn

In response to the interview of September 11, 2007, the examiner herein withdraws the Office Action mailed August 6, 2007 in favor of the instant Office Action, for the reasons set forth below.

Response to Interview

During the interview of September 11, 2007, the examiner recognized that the previous issued Non-final Office action required further clarification and that some rejections presented could be withdrawn in order to simplify the issues as they do not address any additional issues that could not be addressed with fewer rejections.

Additionally, the examiner has determined that both a written description and enablement rejection are necessary, as set forth below. Furthermore, during the interview, Applicant presented arguments asserting that *In re Wiggins* supports certain claim limitations and renders the instant claims patentable. The examiner has chosen to discuss *Wiggins*, to rebut Applicant's assertion in the instant Office Action.

Response to Amendments/Arguments

Applicant's amendments and arguments filed May 16, 2007 are acknowledged. Any rejection and/or objection not specifically addressed is herein withdrawn.

The declaration of Dr. Nardi under 37 CFR 1.132 filed May 16, 2007 is insufficient to overcome the rejections of claims 1, 3, 4, 6, 7, 9, 27 and 28 under 35 USC §§ 102(b), 102(e) and 103(a) as set forth in the last Office action because the declaration provides Applicant's interpretation of the prior art references, but fails to provide evidence that the prior art

compositions, which anticipate the instant claims, or render the composition obvious, would not provide the biological effect claimed to the subject. Here, it is the desmopressin which provides the claimed biological effect, and any composition comprising the requisite concentration of desmopressin will anticipate the claims. During the interview, Applicant asserted that the declaration is fact and not opinion (See Interview summary, e.g. page 7 of 10, last paragraph), however the declaration provides no evidence to support the position that the compositions of the prior art would not function as claimed. Furthermore, the declaration appears to misrepresent the fact that STANLEY (US Patent, 4,863,737) teaches a lollipop containing 20 μg of desmopressin and that the lollipop is intended "to be used in the treatment of the symptoms associated with polyuria," (column 24, Example 20) and that the lollipops are, "capable of absorption through the mucosal tissues of the mouth, pharynx, and esophagus," (abstract), asserting that Stanley teaches primarily a fentanyl lollipop and, "a candy matrix for transmucosal delivery through the mucous membranes of the mouth, pharynx, and esophagus of drugs, including a long list of actives, and desmopressin, which can be present in amounts ranging from 10 to 50 micrograms." (Affidavit 5/16/07, page 7). The affidavit would appear to represent Stanley as providing vague teachings, i.e.- "a long list of actives, and desmopressin, which can be present in amounts ranging from 10 to 50 micrograms," while it in fact Stanley teaches specifically, and unambiguously, the 20 μg desmopressin lollipop, route of administration and intended purpose.

Furthermore, it is well established that "Products of identical chemical composition can not have mutually exclusive properties," and a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties

applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Additionally, the Office does not have the facilities for examining and comparing Applicant's composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

In view of this, and after careful review and consideration of the declaration, the examiner is unable to see a patentable difference between the composition instantly claimed- a pharmaceutical composition comprising 0.5 ng to 20 μg desmopressin and a pharmaceutical carrier in a dosage form adapted for the various routes of administration claimed, and the compositions of the prior art, e.g. the desmopressin lollipop of Stanley.

Furthermore, Applicant's arguments concerning the 35 USC § 102 rejections have been carefully considered but are not deemed to be persuasive of error in the rejections. Applicant argues that the Examiner's position that the administration of the cited prior art desmopressin pharmaceutical compositions would inherently provide the instantly claimed function effect (i.e., establishing a steady state plasma/serum desmopressin concentration) is incorrect because the claims require that concentrations within this range must be established, that is, maintained for some reasonable time, and that underlying the instantly claimed invention is the discovery

that maintenance of such low doses can act effectively to interrupt urine production while decreasing or eliminating induction of hyponatremia. Respectfully, the claims are all drawn to a pharmaceutical product (not to a method of its use) and, as such, the prior art references cited below, would inherently have the instantly claimed functional effect if administered.

Discussion of In re Wiggins

Applicant introduced *In re Wiggins*, 158 USPQ 199, 397 F2d 356 (C.C.P.A. 1968), during the interview and asserted that the fact pattern supports the patentability of the instant claims. Respectfully, the examiner disagrees for the following reasons. First, the rejection set forth in *Wiggins* was under obviousness, and not anticipation, and thus is not directly applicable to the instant rejections. Further, assuming *arguendo* that the decision is applicable to anticipatory rejections, the fact pattern in *Wiggins* differs from the instant claims on all three points of *Wiggins* which led to the patentability determination based upon "a triad of basic negative findings".

The prior art applied in *Wiggins* , Wolf, "found that compound was not a "depressant" or "anaesthetic," that it was otherwise "pharmacologically inert," and that it was unsuccessful on oral application; when considered with reference's apparent failure to suggest applicant's claimed dosage amounts, such a triad of basic negative findings, rather than making applicant's discovery obvious, seems to have opposite effect; it would have had general effect of deterring further experimentation; in light of background of subject matter, content of prior art, and differences between it and applicant's claims, court cannot say that applicant's discovery was obvious to one skilled in the art."

Here, the prior art applied is distinguishable from the fact pattern of *Wiggins* as desmopressin of the instant prior art is well known to be pharmacologically active as an antidiuretic, being used for this very purpose in the art, and thus is clearly not "pharmacologically inert," or unsuccessful in being an antidiuretic. For example, FLOCKHART (US Patent 5,298,256) teaches desmopressin, "can be used with advantage by patients with diabetes insipidus, childhood enuresis and incontinence in general" (column 3, lines 43-45). Furthermore, the prior art clearly and unambiguously teaches desmopressin at the instantly claimed ranges for the composition, and thus does more than, "suggest applicant's claimed dosage amounts," being that it anticipates such claimed ranges of desmopressin, e.g. Stanley, *supra*. Thus, in contrast to *Wiggins*, there is no "triad of basic negative findings" which would deter further experimentation or lead one upon analysis of the *Graham factors* to conclude that the claimed compositions are non-obvious, or unanticipated.

Drawings

The drawings are objected to because the submitted drawings appear to be black and white renditions/copies of color figures, particularly as evidenced by the presence of color drawings in the divisional application 11/744,615. Here, the features of the figures cannot be discerned, as the various lines are of such a style/rendering that identification of a particular line in any figure is difficult. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the

appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Please note- color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 4, 6, 7, 9, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

MPEP § 2163 states that, "[n]ew or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement. See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); *In re Smith*, 458 F.2d 1389,1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads)." Further, the MPEP states, "[w]hile there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure."

Here, the amendments to the claims on May 16, 2007 introduced the new matter, as the new limitation to claim 1 is not supported by explicit, implicit or inherent disclosure in the originally filed specification, claims or drawings. The newly introduced claim limitations provide for a negative proviso that the dosage form "does not produce a desmopressin plasma/serum concentration exceeding about 10 pg/ml,", however such a proviso is not found in the specification explicitly, implicity or inherently. MPEP 2173.05(i) states in part, "Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. *See In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff 'd mem.*, 738 F.2d 453 (Fed. Cir. 1984)."

Here, while there is no *in haec verba* requirement to satisfy the requirement of written description under 35 USC § 112, 1st ¶, there is no basis in the original disclosure that would lead one to conclude that Applicant had originally contemplated disclaiming compositions which cause higher serum/plasma desmopressin concentrations that equilibrate at a later time to the steady state claimed.

During the interview, Applicant suggested making the limitation a dependent claim, in order to retain the limitation for appeal. The examiner would likely apply the same rejection to the dependent claim, as the disclosure does not provide support for the concept that the circulating levels are not to rise above the recited limitation.

Claims 1, 3, 4, 6, 7, 9, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, while being enabling for desmopressin at the specifically defined and exemplified concentrations in the specification having the desired effect, does not reasonably provide enablement for all concentrations within the claimed range. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the

invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The claims are drawn to a pharmaceutical composition comprising 0.5 ng to 20 μg desmopressin and a pharmaceutically acceptable carrier in a dosage form adapted for intranasal, transmucosal, transdermal, or intradermal administration sufficient to establish in a patient a steady plasma/serum desmopressin concentration in the range of from about 0.1 picograms desmopressin per mL plasma/serum to about 10.0 picograms desmopressin per mL plasma/serum and to decrease urine production, with the proviso that said dosage form does not produce a desmopressin plasma/serum concentration exceeding about 10 pg/ml. Thus, the claims embrace any composition (transdermal, transmucosal, intradermal or intranasal) where desmopressin is between 0.5 ng and 20 μg.

Applicant has provided a declaration under 37 CFR § 1.132 which states that the prior art compositions would not provide the required serum/plasma desmopressin concentrations, however the examiner maintains that the prior art compositions anticipate the instant claims, particularly in view of *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977), *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688

(CCPA 1972) and *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990), as the compositions of the prior art are within the claimed range of Applicant. Thus, in view of this dichotomy, one of skill in the art would be unduly burdened to make and use the plurality of compositions within the claimed range beyond those specifically shown in the specification to have the requisite activity, as Applicant states that the identified compositions would not function as instantly claimed even though they are within the specifically claimed range of desmopressin and are adapted for the various routes of administration as claimed and are known to be used for the very same purpose.

Furthermore, the specification provides no specific guidance as to how one would make the compositions which would achieve the requisite pharmacokinetic profile, particularly since the examples are intravenous injection or 'comparative examples' and the examples presented are all outside of the claimed dosage range. The specification provides no guidance as to how one would extrapolate from the intravenous injection solution to intranasal, transmucosal, transdermal or intradermal compositions such that one would achieve the claimed pharmacokinetic profiles. Applicant asserts that such dosage forms, "could be devised by persons of skill in the art to achieve this blood concentration and its unexpected effects." (Interview Summary, page 3 of 10). Clearly, if such pharmacokinetic effects are unexpected, one would understand that this is an unpredictable effect and the level of skill and knowledge in the art, with regards to achieving this 'unexpected' effect, is very low and would require a significant amount of guidance to achieve this effect. Here, the specification provides, at best, guidance for 'trial and error' experimentation, particularly in view of the declaration asserting that none of the prior art compositions, which are desmopressin pharmaceuticals at the requisite

concentration and route of administration, would achieve the claimed result. Again, lacking any working examples of compositions embraced by the instant claims, and lacking sufficient guidance to lead one to compositions which would have the pharmacokinetics profile within the claims, one would be burdened with undue experimentation to make compositions which would achieve the required pharmacokinetics profile as claimed.

Applicant is reminded that, "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See *Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. (*Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 42 USPQ2d 1001 (Fed. Cir. 1997)).

Claims 1, 3, 4, 6, 7, 9, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated that, "To fulfill the written description requirement,

a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated that, "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a pharmaceutical composition comprising 0.5 ng to 20 μg desmopressin and a pharmaceutically acceptable carrier in a dosage form adapted for intranasal, transmucosal, transdermal, or intradermal administration sufficient to establish in a patient a steady plasma/serum desmopressin concentration in the range of from about 0.1

picograms desmopressin per mL plasma/serum to about 10.0 picograms desmopressin per mL plasma/serum and to decrease urine production, with the proviso that said dosage form does not produce a desmopressin plasma/serum concentration exceeding about 10 pg/ml.

Applicant argues in the affidavit, and subsequently in the interview, that the prior art compositions would not achieve the requisite desmopressin serum levels and that the invention "does not lie in the particular way (mechanical or chemical) one achieves the blood concentration range" and that "persons skilled in the art are able to readily to (*sic*) make dosage forms without undue experimentation that can easily achieve establishment of the stated blood concentration range." (Interview Summary, page 6 of 10).

Respectfully, the prior art clearly teaches compositions comprising desmopressin at the required concentration in the composition, and thus under inherency, it must function as claimed, particularly when there is nothing else described in the composition. Absent disclosure of what critical element of the composition allows for the alleged altered bioavailability, Applicant is not in possession of the claimed invention. Applicant's only described composition is an intravenous (i.v.) composition, which has been specifically excluded from the claims. Furthermore, the description of an i.v. solution does not *per se* provide description of compositions administered via other routes such that they would achieve the same results. Clearly, in view of the dichotomy set forth above under enablement, the compositions are insufficiently described such that one would recognize that they were in possession of an infringing composition.

(1) Level of skill and knowledge in the art:

The artisan is knowledgeable of making basic pharmaceutical composition comprising desmopressin at various concentrations. However, in view of Applicant's declaration and arguments coupled with the instant disclosure, the artisan is unknowledgeable as to the *a priori* determination of which compositions will function as claimed.

(2) Partial structure,(3) Physical and/or chemical properties and (4) Functional characteristic:

The compositions must comprise desmopressin and a pharmaceutically acceptable carrier in a dosage form adapted for intranasal, transmucosal, transdermal, or intradermal administration sufficient to establish in a patient a steady plasma/serum desmopressin concentration in the range of from about 0.1 picograms desmopressin per mL plasma/serum to about 10.0 picograms desmopressin per mL plasma/serum and to decrease urine production, with the proviso that said dosage form does not produce a desmopressin plasma/serum concentration exceeding about 10 pg/ml.

However, the claims and specification do not provide for any additional critical elements required to achieve the serum levels. Applicant's arguments assert that such determination is not unduly burdensome and that "many dosage forms could be devised by persons of skill in the art to achieve this blood concentration and its unexpected effect. To protect his invention properly it was critical to obtain low dose desmopressin claims that art unlimited with respect to the chemical or mechanical way the dosage form worked. Rather, the important characteristic of the dosage form is that it is effective to achieve the stated blood concentration range for some desired short period of time, irrespective of how it does so."

While there may be "many dosage forms" that "could be devised", the instant application is absent any single specific embodiment that does function as claimed, being that all of the examples are either routes of administration not claimed (e.g. i.v.) or are 'comparative examples' of compositions, where the formulation is desmopressin at concentrations outside the instant claimed range (e.g. Examples 1-6, Comparative Examples 1-3, etc.). Thus, no single specific composition is described.

(5) Method of making the claimed invention:

As above, methods of making compositions are well known to the artisan, however the artisan would not know which compositions would function as claimed without 'trial and error' experimentation until the desired result is achieved. Furthermore, in view of the disclosure, one would not know where to start, and would not find sufficient guidance to make the compositions with the requisite activity, particularly when the prior art teaches various compositions that have the requisite concentration of desmopressin are asserted by Applicant in the declaration to lack the ability to achieve the serum concentrations.

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that the claims are broad and generic, with respect to all possible compositions encompassed by the claims. The possible structural variations are limitless to any composition 'adapted for' the various claimed routes. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compositions. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus, being void of any single example that functions as claimed, and the

specification does not provide sufficient descriptive support for the myriad of compositions embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 4, 6, 7, 9, 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 4, 6, 7, 9, 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are those elements in the composition that are specifically required to achieve the desmopressin plasma/serum concentrations claimed.

Claims 1, 3, 4, 9, 27 and 28 recite, "from about... to about...", which renders the claims vague and indefinite. "From" and "to" are static limitations and define boundaries, while 'about' is a dynamic limitation and allows for variability, including that which is outside the range recited.

Claim Rejections - 35USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 7, 9, 27, and 28 remain rejected under 35 U.S.C. 102(b) as being anticipated by STANLEY (US 4,863,737).

The instant claims are presented *supra*.

Stanley teaches a pharmaceutical composition lollipop comprising 20 μg of desmopressin and maltodextrin (an 'open matrix network') (see, e.g., col 24, lines 40-61 - Example 20). Stanley teaches that the lollipop is for the treatment of "the symptoms associated with polyuria" (column 24, lines 43-44). Stanley teaches that the compositions are, "capable of absorption through the mucosal tissues of the mouth, pharynx, and esophagus," (abstract), and thus are 'adapted for transmucosal delivery' and buccal administration.

Because the structural limitations are met the steady plasma/serum desmopressin concentration within the approximate instantly claimed range, as well as a decrease in urine production, would inherently occur (especially given that the amount of desmopressin within the referenced desmopressin formulations are within the instantly claimed amount ranges), as it is well established that "Products of identical chemical composition can not have mutually exclusive properties," and a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Additionally, Applicant is reminded that the Office does not have the facilities for examining and comparing Applicant's composition with the composition of the prior art, the

burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Claims 1, 3, 4, 9, 27, and 28 remain rejected under 35 U.S.C. 102(b) as being anticipated by DIXON.

The instant claims are presented *supra*.

Dixon teaches injectable pharmaceutical compositions of desmopressin at 200 ng (0.2 μg), 1 μg and 4 μg (page 485, 1st full ¶). Although the compositions of Dixon were administered intravenously, nothing physically distinguishes such injectable compositions from those administered via intradermal or subdermal injection. Applicant is reminded that the claims are drafted as compositions and nothing precludes one from using it for a different intended use.

Because the structural limitations are met the steady plasma/serum desmopressin concentration within the approximate instantly claimed range, as well as a decrease in urine production, would inherently occur (especially given that the amount of desmopressin within the referenced desmopressin formulations are within the instantly claimed amount ranges), as it is well established that "Products of identical chemical composition can not have mutually exclusive properties," and a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed.

Cir. 1990). Additionally, Applicant is reminded that the Office does not have the facilities for examining and comparing Applicant's composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Art Pertinent to Applicant's Claimed Invention

Additional references which have not been previously cited on any PTO-892 or PTO-1499 are identified below as being pertinent to the instant claims:

CORT (US Patent 4,263,283) teaches a desmopressin composition for intranasal administration (nose drops). The administered dose is about 10 μg (0.1 ml of a 100 μg/ml solution) and is administered every 3 to 6 hours (column 2, lines 30-33), "the concentration of desmopressin in the solution is not narrowly critical, and can range from about 1 μg/ml to 1000 μg/ml or higher, depending on the intended mode of administration and dosage." (column 2, lines 44-47). And that, "injectable solutions will contain of the order of about 4 to about 10 μg desmopressin per milliliter." (column 2, lines 53-55).

MEDSAFE ("MINIRIN NASAL SPRAY". Ferring Pharmaceuticals. Internet document <<http://www.medsafe.gov.nz/Consumers/CMI/m/MinirinNSpray.htm>>, May 3, 2001; accessed 10/4/07; 3 pages) teaches desmopressin nasal spray having 10 mcg/dose and being used for night time bedwetting and diabetes insipidus (page 1 of 3).

FLOCKHART (US Patent 5,298,256) teaches desmopressin in a buccal patch (e.g. column 5, line 41+).

HARRIS (US Patent 5,482,931) teaches desmopressin nasal spray (e.g. Example 1).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Andrew D. Kosar
Patent Examiner
Art Unit 1654